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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/680,996	10/07/2003	William G. Tatton	17530 (AP)	6653

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Carlos A. Fisher
ALLERGAN, INC.
T2-7H
2525 Dupont Drive
Irvine, CA 92612

EXAMINER	
CLAYTOR, DEIRDRE RENEE	

ART UNIT	PAPER NUMBER
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	**Application No.** 10/680,996	**Applicant(s)** TATTON ET AL.	
	Examiner Renee Claytor	**Art Unit** 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2003*.
2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.
3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.
  4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5)☐ Claim(s) _____ is/are allowed.
6)☒ Claim(s) *1-6* is/are rejected.
7)☐ Claim(s) _____ is/are objected to.
8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.
10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.
  Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
  Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  a)☐ All b)☐ Some * c)☐ None of:
    1.☐ Certified copies of the priority documents have been received.
    2.☐ Certified copies of the priority documents have been received in Application No. _____.
    3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
  * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/10/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

This application claims priority to U.S. Provisional Application 60/417,031, filed on 10/8/2002. Applicant's priority is acknowledged.

Claim Objections

Claim 3 objected to because of the following informalities: "locus sereleous" should be spelled "locus ceruleus". Appropriate correction is required.

Claim Rejections – 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and 6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating Parkinson's disease and Alzheimer's disease, does not reasonably provide enablement for the treatment of all neurodegenerative disorders . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The Nature of the Invention: The rejected claims 1-3 and 6 are drawn to a method for treating a neurodegenerative disorder comprising administration of the α_2-receptor agonist brimonidine.

(2) The state of the prior art: The state of the art regarding treating neurodegenerative disorders is relatively high (Hilbush, B.S. et al., NeuroRx: The Journal of the American Society for Experimental NeuroTherapeutics, 2, 627-37, 2005). However the state of the art for the treatment of neurodegenerative disorders with the α_2-receptor agonist brimonidine is underdeveloped. The skilled artisan would view that the treatment of all neurodegenerative disorders with brimonidine is highly unlikely.

(3) The relative skill of those in the art: The relative skill of those in the art is high.

(4) The breadth of the claims: Claims 1-3 and 6 embraces a method for the treatment of neurodegenerative conditions comprising administration of the α_2-receptor agonist brimonidine.

(6) The amount of guidance or direction presented: In the instant case, working examples are presented for treating the neurodegenerative conditions Alzheimer's disease and Parkinson's disease with brimonidine, outlined in the specification on pages 41-47. As a result of the treatment, animal models of neuron impairment in Parkinson's disease and Alzheimer's disease were shown to be improved after administration of brimonidine; however, there are a lack of working examples presented in the specification as filed showing how to treat all neurodegenerative conditions. Note that lack of a working example is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP § 2164.

(7) The presence or absence of working examples: Applicant provides working examples for treating animal models of neuron loss in Parkinson's disease and Alzheimer's disease. However, applicant does not provide any working examples for all neurodegenerative conditions.

(8) The quantitation of experimentation necessary: Claims 1-3 and 6 read on a method for treating neurodegenerative conditions with the α_2-receptor agonist brimonidine. As discussed above, the specification provides examples for treating neuron loss in Parkinson's disease and Alzheimer's disease, but the specification fails to provide sufficient support for treating all neurodegenerative conditions. Applicant fails to provide information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Claims 3 and 6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for decreasing the amount of neuron loss following brimonidine treatment, does not reasonably provide enablement for preventing death or degeneration of neurons. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The Nature of the Invention: The rejected claims 3 and 6 are drawn to a method of treatment of neurodegenerative conditions by preventing death or degeneration of neurons projecting to or from the ventral tegmental area, the locus ceruleus and the substantia nigra.

(2) The state of the prior art: The state of the art regarding treating neurodegenerative conditions is relatively high (Hilbush, B.S. et al., NeuroRx: The Journal of the American Society for Experimental NeuroTherapeutics, 2, 627-37, 2005). However the state of the art for preventing the death or degeneration of neurons is underdeveloped.

(3) The relative skill of those in the art: The relative skill of those in the art is high.

(4) The breadth of the claims: The claims 3 and 6 embrace treating neurodegenerative conditions by preventing death or degeneration of neurons projecting to or from the ventral tegmental area, the locus ceruleus and the substantia nigra.

(5) The amount of guidance or direction presented: In the instant case, no working examples are presented in the specification as filed showing how to prevent the death or degeneration of neurons. Note that lack of a working example is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP § 2164. The specification on pages 41-47 details studies performed in mouse models administered MPTP to cause significant neuron loss in the substantia nigra and ventral tegmental area. Of these animals, one group was administered brimonidine, which attenuated the MPTP-induced damage but did not prevent it.

(6) The presence or absence of working examples: Applicant does not provide any working examples for the prevention of death or degeneration of neurons projecting to or from the ventral tegmental area, the locus ceruleus and the substantia nigra.

(7) The quantitation of experimentation necessary: Claims 3 and 6 read on the treatment of neurodegenerative conditions by preventing death or degeneration of neurons projecting to or from the ventral tegmental area, the locus ceruleus and the substantia nigra. As discussed above, the specification provides examples for attenuating neuron loss in the neurodegenerative conditions of Parkinson's disease and Alzheimer's disease, but the specification fails to provide sufficient support for the prevention of neuron loss in the neurons projecting to or from the ventral tegmental area, the locus ceruleus and the substantia nigra. Applicant fails to provide information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

> the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3 and 5-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Arnsten et al. (Science, Vol. 230; pgs. 1273-1276) in view of Olejnik et al. (U.S. Patent 6,627,210).

Arnsten et al. teach that there is a loss of catecholamines in Alzheimer's disease and that pharmacological treatments may ameliorate the cognitive deficits (pg. 1274, Col. 1 and 2). Arnsten et al. teach that the α_2-receptor agonist clonidine caused memory improvements in animal models of dementia (pg. 1274, Col. 3, second paragraph) and further teach that adrenergic agonists will be helpful for patients with Alzheimer's disease (meeting the limitation of claims 1, 3, and 6; pg. 1276, Col. 2). Systemic administration was achieved by intramuscular injections and oral administration (meeting the limitation of claim 2; #11 in References and Notes). It is taught that cell deterioration occurs in the locus ceruleus (meeting the limitation of claims 3 and 6; pg. 1276, Col. 2).

Arnsten et al. do not teach brimonidine as the α_2-receptor agonist.

Olejnik et al. teach compositions comprised of α_2-receptor agonists as the active ingredient, with the preferred α_2-receptor agonist being briminodine (Col. 5, lines 45-48 and claim 1). Other suitable α_2-receptor agonists include clonidine (Col. 5, line 26).

Accordingly, it would be obvious to one having ordinary skill in the art at the time of the invention, to use the α_2-receptor agonist briminodine as taught by Olejnik et al. in the invention of Arnsten et al. One having ordinary skill in the art would have been motivated to do so because it is taught that both clonidine and briminodine are both α_2-receptor agonists and a reasonable expectation of success of treating age-related dementia or Alzheimer's would be expected.

Claim 4 rejected under 35 U.S.C. 103(a) as being unpatentable over Arnsten et al. (Science, Vol. 230; pgs. 1273-1276) in view of Olejnik et al. (U.S. Patent 6,627,210) as applied to claims 1-3 and 5-6 above and in further view of Chan-Palay et al. (The Journal of Comparative Neurology, 287: 373-392).

Arnsten et al. and Olejnik et al. teach α_2-receptor agonists that treat Alzheimer's disease.

Arnsten et al. and Olejnik et al. do not teach that α_2-receptor agonists treat Parkinson's disease.

Chan-Palay et al. teach that the locus ceruleus is an important source of norepinephrine and is shown to be affected in several neurologic disorders, including Parkinson's disease and Alzheimer's disease (pg. 373, first paragraph).

Accordingly, it would have been obvious to one having ordinary skill in the art at the time of the invention to utilize an α_2-receptor agonist in the treatment of Parkinson's disease because Chan-Palay et al. teach that the locus ceruleus is involved in Parkinson's disease. One would have been motivated to treat Parkinson's disease with brimonidine because Chan-Palay et al. teaches that norepinephrine in the locus ceruleus is implicated in Parkinson's and Alzheimer's disease, and Arnsten et al. and Olejnik et al. teach that cell deterioration occurs in the locus coeruleus in Alzheimer's disease and that α_2-receptor agonists (including brimonidine) are a beneficial treatment for Alzheimer's disease. There would be a reasonable expectation of success according to the prior art teachings because both diseases have similar pathologies.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8, 10, 13-15 of copending Application No. 10/680,879. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to a method for treating a neurodegenerative condition of the brain comprising administering an effective amount of brimonidine. The claims of Application No. 10/680,879 are likewise drawn to a method for treating neurodegenerative conditions of the brain comprising administration of an effective amount of a selective alpha 2B or alpha 2B/2C adrenergic receptor agonist. Both Applications are drawn to a method of treating neurodegenerative conditions by administering an alpha 2 receptor agonist; therefore, it would be obvious to use the alpha 2 receptor agonist briminodine from the claimed invention as the alpha 2B or alpha 2B/2C adrenergic receptor agonist of Application No. 10/680,879.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Renee Claytor whose telephone number is 571-272-8394. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Renee Claytor

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER